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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/531,552	11/08/2005	Jerome B Zeldis	9516-075-999	3548

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JONES DAY
222 E. 41ST. STREET
NEW YORK, NY 10017

EXAMINER	
BETTON, TIMOTHY E	

ART UNIT	PAPER NUMBER
1627	

MAIL DATE	DELIVERY MODE
02/19/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/531,552	ZELDIS, JEROME B	
	Examiner	Art Unit	
	TIMOTHY E. BETTON	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-9,13,14 and 38-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-9,13,14 and 38-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments filed on 3 October 2009 has been acknowledged and duly made of record.

Status of the Claims

Claims 1, 3, 5-9, 13-14, 38-50 are pending further prosecution on the merits.

Response to Arguments

The rejections under 35 U.S.C. § 112 have been withdrawn in view of current amendments to claims 1, 3, 4-10, and 13-25 drawn to prevention and claims 1-10 and 15-25 drawn to lack of enablement to treat any MDS disorder.

Applicant's arguments see current Remarks by applicant on pages 7-9, filed 26 June 2009, with respect to the Double Patenting Rejections have been fully considered and are persuasive. The application 11/250,408, 11/818,927 and patent 6,020,358 of current Double Patenting Rejection has been withdrawn.

Applicant's arguments, see pages 10-11 of said Remarks , filed 26 June 2009, with respect to the rejection(s) of claim(s) 1-10 and 15-25 under Muller *et al.* (U.S. Patent 6,020,358, "the '358 patent") and Muller *et al.* (U.S. Patent 5,658,940, "the '940 patent") in view of Raza *et al. (Hematology* 5(4):275-284, 2000, "Raza"); in view of Celgene Corporation Annual Report, 12/31, 2000, pp. 1-165 ("Celgene Report"); and further in view of Muller *et al.* (U.S. Patent 5,605,914, "the '914 patent") (Office Action, pages 15-17) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the new rejection below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5-9, 13-14, 38-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In re Wands, set forth the following eight factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph:

1) the quantity of experimentation necessary
2) the amount of direction or guidance provided
3) the presence or absence of working examples
4) the nature of the invention
5) the state of the art
6) the relative skill of those in the art
7) the predictability of the art and
8) the breadth of the claim

The breadth of the claims are drawn to a method of treating a MDS with an effective amount of the solvate of cyclopropanecarboxylic acid {2-[1-(3- ethoxy-4-methoxy-phenyl)-2-

methanesulfonyl-ethyl]-3-oxo-2, 3-dihydro-1 H-isoindol-4-yl}-amide and an effective amount of dexamethasone as the second active agent.

The nature of the invention is drawn to the treatment of an array of MDS disorders in the primary stage of development.

The state of the art is replete with ongoing development in order to address the primary stages of MDS that invariably progress to more acute stages of MDS.

The absence of working models disclosing a treatment modality for a patient with primary MDS with the title compound cyclopropanecarboxylic acid {2-[1-(3- ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2, 3-dihydro-1 H-isoindol-4-yl}-amide let *alone the solvate thereof* is no where represented in the whole current specification. Page 21 of the specification discloses the elected compound, however any representation of this title compound in solvate form is silent. Further, in the specification the term solvate is distinct from the term hydrate. According to newly added claim 50, the solvate is a hydrate. However, the specification does not support and/or suggest this synonymous association between a solvate and a hydrate. In the variable listings within the specification, the term hydrate is listed as a distinct entity from a solvate.

Vippagunta et al. (Crystalline Solids, Adv Drug Deliv Rev 2001 May 16; 48(1): 3-26) teach [that] [m]any drugs exist in the crystalline solid state due to reasons of stability and ease of handling during the various stages of drug development. Crystalline solids can exist in the form of polymorphs, solvates or hydrates. Phase transitions such as polymorph interconversion, desolvation of solvate, formation of hydrate and conversion of crystalline to amorphous form

may occur during various pharmaceutical processes, which may alter the dissolution rate and transport characteristics of the drug. Hence it is desirable to choose the most suitable and stable form of the drug in the initial stages of drug development. The current focus of research in the solid-state area is to understand the origins of polymorphism at the molecular level, and to predict and prepare the most stable polymorph of a drug. The recent advances in computational tools allow the prediction of possible polymorphs of the drug from its molecular structure. Sensitive analytical methods are being developed to understand the nature of polymorphism and to characterize the various crystalline forms of a drug in its dosage form. The aim of this review is to emphasize the recent advances made in the area of prediction and characterization of polymorphs and solvates, to address the current challenges faced by pharmaceutical scientists and to anticipate future developments.

Thus, the limitation of claim 50 drawn to the *solvate as a hydrate* is not supported in the specification. Further, the teachings of Vippagunta further elucidate the lack of enablement that is apparent via the absence of the current specification teaching the solvate form of the title compound cyclopropanecarboxylic acid {2-[1-(3- ethoxy-4-methoxy-phenyl)-2-methanesulfonyl-ethyl]-3-oxo-2, 3-dihydro-1 H-isoindol-4-yl}-amide *let alone this same solvate as a hydrate*.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY E. BETTON whose telephone number is (571)272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1627